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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,492	04/30/2001	Hiroshi Yamamoto	19036/37023	2621

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,492	YAMAMOTO ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *22-30* is/are withdrawn from consideration.

5)☒ Claim(s) *13 and 16* is/are allowed.

6)☒ Claim(s) *1-12, 14, 15 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 12/04/02 (Paper No. 12), is acknowledged.

Claims 1-30 are pending.

Claims 22-30 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-21 are under examination as they read on an antibody having specificity to intracelllular domains of two or more kinds of protein tyrosine phosphatases.

4. The following new grounds of rejections are necessitated by the amendment filed on 12/4/02, paper No. 12.

5. Applicant's IDS, filed 12/04/02 (Paper No. 14), is acknowledged, however, the A1 and C8 references were crossed out because the Office considers the application A1 provided on the 1449 to be subject to 35 USC 122 requiring that the application be kept in confidence since it is not clear that all inventors of the cited application agree that the contents of that application should become publicly available. As for reference C8 the English translation was not provided. Applicant is invited to produce the English translation of C8 reference.

6. Applicant is advised that should claim 1 be found allowable, claim 7 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

8. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "preparing a hybridoma cell line from an antibody-producing cell obtained from the immunized animal; and producing a monoclonal antibody from the hybridoma cell line" claimed in claims 17 and 18 represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 12-4-02 does not point to the specification for support for the newly added limitations "preparing a hybridoma cell line from an antibody-producing cell obtained from the immunized animal; and producing a monoclonal antibody from the hybridoma cell line" as claimed in claims 17 and 18. However, the specification does not provide a clear support of "preparing a hybridoma cell line from an antibody-producing cell obtained from the immunized animal; and producing a monoclonal antibody from the hybridoma cell line". The instant claims now recite limitations which were not clearly disclosed in the specification and claims as originally filed.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-12, 14-15 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeuchi *et al* (Tissue Antigens, 42:441, 1993 IDS Ref. No. C10) as is evidenced in the specification on page 16 of the Sequence Listing under SEQ ID NO: 4 (<210> 4) or Besco *et al* (BMC Genomics. 2:1, 2001) and Bost *et al* (Immuno. Invest. 1988 ;17:577-586) or Bendayan (J. Histochem. Cytochem. 1995, 43:881-886).

Takeuchi *et al* teach the AE-6 monoclonal antibody that recognizes VHCSAGV sequence in CD45 PTPASE (see the abstract on page 441). Takeuchi *et al* further teach that AE-6 monoclonal antibody recognizes cytoplasmic antigen on CD45 (see Abstract). Finally, Takeuchi *et al* teach that using VHCSAGV-KLH as a fusion protein to immunize mice, then the immuminzed spleen cells were fused with NS-1 cells. Positive clones were screened with their reactivity to VHCSAGV-BSA by ELIZA. A clone AE-6 was found to show greatest reactivity (Abstract). As is evidenced in the specification on page 16 of the Sequence Listing under SEQ ID NO: 4 (<210> 4) discloses that SEQ ID NO: 4 V**VHCSAGV**GRTG is identical sequence in phosphatase domain 1 of LAR and CD45. Similarly, Besco *et al* teach that **VHCSAGV,** which is part of the catalytic core of the phosphatase, is highly conserved sequence in LAR and CD45 (see page 8 under Phosphatase domains in particular). Therefore, the monoclonal antibody against VHCSAG recognizes both CD45 and LAR phosphatase domain I.

As is evidenced by Bost *et al* that teach that an antibody specifically bound an epitope shared by two different polypeptides, but did not bind irrelevant peptides not sharing this epitope. The epitope was determined to be a homologous sequence in the two proteins in which 4 of 6 residues were identical (see entire document, but especially the Abstract, Discussion, and "Results", page 579).

Similarly, Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) characterizes the specific reactivity of a monoclonal antibody produced to human proinsulin, and shows that although the antibody is highly specific, it is nevertheless able to bind to not only human proinsulin, but to proinsulin from other species and even a distinct protein, glucagons, based upon conservation of an Arg-Arg dipeptide sequence in each of these molecules (see entire document).

Claim 6 is included because VHCSAGV is a polypeptide that is encoded by a nucleotide of SEQ ID NO:1 at positions (NA 4,976-4,997).

Claims 8-12 are included because an antibody is the same antibody irrespective of how it is made. Further, the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir 198) see MPEP 2113.

Claim 14 is included because the moleculare weight of 146 kDa would be an inherient property of the monoclonal antibody that has specificity to intracelluar domains.

The reference teachings anticipate the claimed invention.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takeuchi *et al* as is evidenced in the specification on page 16 of the Sequence Listing under SEQ ID NO: 4 (<210> 4) or Besco *et al* (BMC Genomics. 2:1, 2001) and Bost et al (Immuno. Invest. 1988 ;17:577-586) or Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) in view of U.S. Patent No.5,736,149 (PTO-892 Ref No. A).

The teachings of Takeuchi *et al,* Besco *et al,* Bost *et al* and Bendayan references and the specification disclosure have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of a method of generating an antibody such as GST-fusion protein as immunogen, preparing a hybridoma cell line from an antibody-producing cell obtained from the immunized animal and producing a monoclonal antibody from the hybridoma cell line in claim 18.

The '149 patent teaches mouse antibodies specific for a GST-fusion protein antigens were prepared by immunizing an animal (i.e. mouse) with a purified GST-fusion protein, bled the animal, and screened for binding to Western blots with the antigens and the animal was selected on the basis of this serum binding. The '149 patent further teaches the said animal spleen cells were harvested and fused with a myeloma cell line, resulting result in mouse antiboides specific for the GST fusion protien antigens (column 18, lines 5-28 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to link the VHCSAGV peptide taught by Takeuchi *et al* with GST- to make a GST-VHCSAGV fusion protein to generate monoclonal antibodies to GST-VHCSAGV fusion protein as taught by Takeuchi *et al* using the method of immunizing an animal with GST-fusion protein taught by the '149 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the mouse immunization with the fusion protein will result in mouse antiboides specific for the GST fusion protien antigens as taught by '149 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takeuchi *et al* as is evidenced in the specification on page 16 of the Sequence Listing under SEQ ID NO: 4 (<210> 4) or Besco *et al* (BMC Genomics. 2:1, 2001) and Bost et al (Immuno. Invest. 1988 ;17:577-586) or Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) in view of U.S. Patent No.5,736,149 (PTO-892 Ref No. A).

The teachings of Takeuchi *et al,* Besco *et al,* Bost *et al* and Bendayan references, '149 patent and the specification disclosure have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation that the method of generating an antibody comprises the step of screening antibodies generated in the immunizing step using said fusion protein in claim 21.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to link the VHCSAGV peptide taught by Takeuchi *et al* with GST- to make a GST-VHCSAGV fusion protein to generate monoclonal antibodies to GST-VHCSAGV fusion protein as taught by Takeuchi *et al* using the methods of immunizing and screening taught by the '149 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because screening antibodies with the fusion protien would allow for the animal selection on the basis of the serum binding as taught by '149 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takeuchi *et al* as is evidenced in the specification on page 16 of the Sequence Listing under SEQ ID NO: 4 (<210> 4) or Besco *et al* (BMC Genomics. 2:1, 2001) and Bost et al (Immuno. Invest. 1988 ;17:577-586) or Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) in view of U.S. Patent 5,736,149 as applied to claim 18 and further in view of U.S. Patent 5,837,505 (PTO-892 Ref. No. C).

The teachings of Takeuchi *et al,* Besco *et al,* Bost *et al* and Bendayan references, the specification disclosure and the '149 patent have been discussed, supra.

The claimed invention further differs from the reference teachings only by the recitation that the GST-LAR phosphatase domain fusion protein is produced by culturing transformed Escherichia coli at 20-30°C for 16-24 hours.

The '505 patent teaches that plasmids were transformed into E. coli, cultured overnight at 30°C Column 20, lines 1-5). The 30°C temperature is within the 20-30°C range and overnight overlaps with 16-24 hours range. The '505 patent further teaches that using E. coli expression system offers many advantages including a higher rate of transformation, subsequent ease of DNA extraction, and manipulations of subcloning, mapping and DNA sequencing (column 14, lines 26-32).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to link the VHCSAGV peptide taught by Takeuchi *et al* with GST- to make a GST-VHCSAGV fusion protein to generate monoclonal antibodies to GST-VHCSAGV fusion protein as taught by Takeuchi *et al* using the method of immunizing an animal with GST-fusion protein taught by the '149 patent, wherein the fusion protein is produced by transforming E. coli with GST-LAR fusion gene as taught by the '505 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because E. coli expression system offers many advantages including a higher rate of transformation, subsequent ease of DNA extraction, and manipulations of subcloning, mapping and DNA sequencing as taught by '505 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takeuchi *et al* as is evidenced in the specification on page 16 of the Sequence Listing under SEQ ID NO: 4 (<210> 4) or Besco *et al* (BMC Genomics. 2:1, 2001) and Bost et al (Immuno. Invest. 1988 ;17:577-586) or Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) in view of U.S. Patent 5,736,149 as applied to claim 18 and further in view of U.S. Patent 5,837,505 (PTO-892 Ref. No. C) as applied to claim 19 above, and further in view of Hersh *et al* (PTO-892 Ref. No. X) and Harlow *et al* (PTO-892 Ref. No. W).

The teachings of Takeuchi *et al,* Besco *et al,* Bost *et al* and Bendayan references, the specification disclosure and the '149 and `505 patents have been discussed, supra.

The claimed invention further differs from the reference teachings only by the recitation that the GST-LAR phosphatase domain fusion protein is purified based on affinity and elution of said fusion protein is performed by boiling in presence of a detergent.

Hersh *et al* teach lysates were cleared overnight by incubation with glutathione-Sepharose beads, either purified GST-fusion protein or GST was added to an equal aliquot of cell lysate and incubated overnight. Proteins were eluted from the beads by boiling in SDS/PAGE sample buffer. Samples were used for antibody binding assays (page 2398, right column 1st paragraph).

Harlow *et al* teaches that depending on the source of the pure antigen, individual preparations may have unusual buffers, high or low pH, or denaturants (page 60, 2nd paragraph in particular). Harlow further teaches denatured antigen results in antibodies are good for techniques that need or benefit from denaturation-specific antibodies (e.g. Western blots).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to link the VHCSAGV peptide taught by Takeuchi *et al* with GST- to make a GST-VHCSAGV fusion protein to generate monoclonal antibodies against GST-VHCSAGV fusion protein as taught by Takeuchi *et al* using the method taught by the '149 patent wherein the fusion protein is produced by transforming E. coli with GST-LAR fusion gene as taught by the

'505 patent and elution of said fusion protein using boiling in presence of a detergent as taught by Hersh *et al* and use as denatured antigen as taught by Harlow *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because purified denatured antigen results in antibodies that are good for techniques that need or benefit from denaturation-specific antibodies (e.g. Western blots) as taught by Harlow et al.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-3, 6-12, 14-15 and 17-21 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10, 12-13 and 15-19 of copending Application No. 09/719,272.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-10, 12-13 and 15-19 of the 09/719,272 application and claims 1-3, 6-12, 14-15 and 17-21 of the instant application are considered to be claiming substantially the same antibody having specificity to intracellular LAR phosphatase and methods of producing said antibodies.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 1-3, 6-12, 14-15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Debant *et al* (IDS Ref. No. U) in view of U.S. Patent No. 4,752,583 (IDS Ref. No. B).

Debant *et al* teach an anti-LAR (cytoLAR) polyclonal antibody, which was isolated from rabbit, immunized with LAR intracellular region protein amino acids 1275-1881 (page 5467, left column, 3rd paragraph in particular). The referenced LAR intracellular region consists of two phasphatase domains D1 and D2 (page 5468, Figure 1 in particular).

The claimed invention differs from the reference teachings only by the recitation that the antibody is monoclonal antibody in claims 1 and 7, A hybridoma cell line in claim 15, and a method of generating an antibody comprising immunizing an animal with a fusion protein that comprises a protein tyrosine phosphatase domain and another protein or a polypeptide fragment; preparing a hybridoma cell line from an antibody-producing cell obtained from the immunized animal in claim 17.

The '583 patent teaches a method of producing monoclonal antibody comprises immunizing a suitable animal with a protein or peptide antigens, obtaining from the animal sensitized spleen cells or lymphocytes capable of producing antibodies to the antigen of choice, fusing the sensitized spleen cells with myeloma cells of the same species or of another animal species, culturing the hybrid cells in a suitable host or in a culture medium, isolating clones of hybrid cells (hybridomas) which continuously produce specific antibodies to the antigen, selecting hybridomas which produce these monoclonal antibodies, producing these antibodies in the culture medium or in a host and harvesting the antibodies from the culture medium or from the host used for growing the cells (column 3, lines 44-65 in particular). The '583 patent further teach that monoclonal antibodies produced exhibit high degree of specificity and greater affinity (column 4, lines 64-65 in particular).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce monoclonal antibody using the method taught by the '583 patent against intracellular phosphatase domains taught by Debant *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to make monoclonal antibody against LAR intracellular region protein because the '583 patent teaches that monoclonal antibodies exhibit high degree of specificity and greater affinity.

Claim 6 is included because the referenced antibody is generated using amino acid 1275-1881 of LAR intracellular domains, whereas a fragment (aa 1291-1881) of LAR polypeptide is encoded by the claimed nucleotide sequence SEQ ID NO:1 (see attached sequence alignment). Therefore, the referenced antibody would recognize the polypeptide encoded by SEQ ID NO: 1.

Claims 8-12 are included because an antibody is the same antibody irrespective of how it is made.

Claim 14 is included because the moleculare weight of 146 kDa would be an inherient property of the monoclonal antibody that has specificity to intracelluar domains.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 12/04/02 (Paper No. 12), have been fully considered, but have not been found convincing.

Applicant argues that Debant *et al* do not teach monoclonal antibodies to the intracellular domains of protein tyrosine phosphatases. Applicant further argue that there is no suggestion or motivation to modify or combine any of these references, while the `583 patent may teach that monoclonal antibodies exhibit a high degree of specificity and greater affinity than polyclonal antibodies, that does not provide a motivation to develop and use monoclonal antibodies in all situations, as evidenced by Debant *et al.*, where the use of anti-LAR polyclonal antisera was sufficient for Debant *et al* 's purposes.

Contrary to Applicant assertion, Dbant *et al* teach a polyclonal antibody against CytoLAR. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991) (discussed below). Although Ex parte Levengood, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done " (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention.

19. Claims 17-18 and 21 stamd rejected under 35 U.S.C. 103(a) as being unpatentable over Debant *et al* in view of U.S. Patent No.5,736,149 essentially for the same reasons set forth in the previous Office Action, paper No. 10, mailed 5/29/02.

Applicant's arguments, filed 12/04/02 (Paper No. 12), have been fully considered, but have not been found convincing.

Applicant argues that the amended claim 1 recite a "monoclonal" antibody, from which claims 17-18 and 21 depend, and hence none of the references cited by the Examiner, alone or in combination, including the `149 patent, account for all elements of any of the claims 17, 18, or

21. Further, none of the references cited by the Examiner, including the `149 patent, provide a suggestion to combine the references to collectively disclose all the elements of any of claims 17, 18 and 21.

Contrary to Applicants assertions, the combined references teach a method of generating a monoclonal antibody using the intracellular domains of LAR as a GST fusion protein.

It is noted that specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA).

In response to applicant's argument that the references fail to show all the elements of applicant's invention, it is noted that those elements are not pointed out in the in Applicant's argument.

20. Claim 19 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Debant *et al* (1996) as applied to claim 18 and further in view of U.S. Patent 5,837,505 essentially for the same reasons set forth in the previous Office Action, paper No. 10, mailed 5/29/02.

Applicant's arguments, filed 12/04/02 (Paper No. 12), have been fully considered, but have not been found convincing.

Applicant argues that cliam 1 as amended recite a "monoclonal" antibody, from which claim 19 ultimately depends. Accordingly, none of the references cited by the Examiner, alone or in cobination, including the `505 patent, disclose all of the elements of claim 19. Applicant further argue that none of the references cited by the Examiner, including the `505 patent, provide a suggestion or motivation to cobine the refereces to collectively disclose all of the elements of claim 19.

Contrary to Applicants assertions, the combined references teach a method of generating a monoclonal antibody using the intracellular domains of LAR as a GST fusion protein and further screening the antibodies using the fusion protein.

21. Claim 20 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Debant *et al* (1996) in view of U.S. Patent 5,736,149 as applied to claim 18 and further in view of U.S. Patent 5,837,505 as applied to claim 19 above, and further in view of Hersh *et al (*March 1999*)* and Harlow et al essentially for the same reasons set forth in the previous Office Action, paper No. 10, mailed 5/29/02.

Applicant's arguments, filed 12/04/02 (Paper No. 12), have been fully considered, but have not been found convincing.

Applicant argues that cliam 1 as amended recite a "monoclonal" antibody, from which claim 20 ultimately depends. Accordingly, none of the references cited by the Examiner, alone or in cobination, including the Hersh *et al* and Harlow *et al*, disclose or suggest all of the elements of claim 20. Applicant further argue that Hersh *et al* and Harlow *et al* do not demonstrate that the techniques reported in those references would be successful in relation to the specific subject matter of the present invention.

In contrast to applicant's assertion that it would be merely an invitation to experiment for antibodies directed to the intracellular LAR phosphatase domain taught by Debant *et al*; no objective evidence has been provided to indicate that the art known process of generating antibodies, including generating monoclonal antibodies for over the past 20 years, to polypeptides of interest would not be successful given the prior art teaching.

22. The declaration of biological deposit, filed 12/4/02 (Paper No. 15), is sufficient to overcome the previous rejection of the instant claims 13 and 16 based upon the deposit of biological materials under 35 U.S.C. § 112, first paragraph.

23. Claims 13 and 16 are allowed.

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
January 27, 2003

Christina Chan

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